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Title Pharmacokinetic advantage of intraperitoneal injection of docetaxel in the treatment fo dissemination of cancer in mice

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Author(s) Tsutomu Shimada[1],Masaaki Nomura[2],Koichi Yokogawa[3],Yoshio Endo[4],Takuma Sasaki[5],Ken-ichi Miyamoto[6],Yutak

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Abstract Intraperitoneal administration of docetaxel has been used to treat peritoneal dissemination of cancer, but its safety h confirmed. We have compared the pharmacokinetic behaviour of docetaxel after intravenous and intraperitoneal adr nu/nu mice bearing MKN45P, a gastric cancer variant line producing peritoneal dissemination. Docetaxel (8 mg kg-1 or intraperitoneally injected into the mice and at designated times the drug concentration was measured in plasma, a abdominal tissues (liver, kidney, intestine and spleen, solid cancer, and suspended free cancer). The pharmacokine docetaxel was similar in control mice and cancer-bearing mice after administration via either route, except that the tr from the abdominal cavity to systemic blood (plasma) was slower in cancerbearing mice than in control mice. As exp intraperitoneal drug concentration was much higher (approximately 100-fold) and was maintained for a longer time i injection group than in the intravenous injection group. The drug concentrations in peritoneal solid cancer tissue and cancer cells were also significantly higher for a longer time in the intraperitoneal injection group than in the intravenc The values of the plasma area under concentration-time curves (AUC) were similar for both administration routes. Tl ascite/AUC plasma after intraperitoneal administration was higher than after intravenous administration. The drug co abdominal organs after intraperitoneal injection was lower during the first 2 h, then became similar to those after intr These results indicated that the intraperitoneal administration of docetaxel for peritoneal dissemination was likely to treatment method, without causing any increase in systemic toxicity.